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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,427	MEIJER ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) *41-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment, filed 22 June 2006, has been entered in full. The amendment, filed 15 October 2009, has been entered in full. Claim 1 is amended.

Applicant's election with traverse of Group I (claims 1-40) in the reply filed on 15 October 2009 is acknowledged. The traversal is on the ground(s) that Applicant has now amended claim 1 such that the claim now recites that "the at least one first cell or tissue is from a first cell type and the at least one second cell or tissue is from a second cell type, and wherein the first cell type is different from the second cell type". Applicant argues that the indicated feature now added by the amendment to claim 1 is not taught by the Goldberg et al. reference.

Applicant's arguments have been fully considered but are not deemed persuasive. **Applicant cannot compare newly amended claim 1 to Goldberg et al., when the Restriction/Election, lack of unity and art of record were clearly made on claim 1 as recited in the previous Office Action.** Previous claim 1 encompassed the first and the second cell being identical. Furthermore, the Examiner has applied art against newly amended claim 1, which supports the lack of unity (no special technical feature).

The requirement is still deemed proper and is therefore made FINAL. Claims 41-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 15 October 2009. Claims 1-40 are under examination.

Priority

Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy (03029541.4) has been placed of record in the file.

Information Disclosure Statement

The information disclosure statement(s) (IDS) (filed 22 June 2006) was received and complies with the provisions of 37 CFR §§1.97, 1.98 and MPEP § 609. The Examiner has provided the missing Foreign Patent Documents and the cited references. They have been placed in the application file and the information referred to therein has been considered as to the merits. It is noted that lined references which state "considered do not print" have been considered by the Examiner, but will not be printed on the face of the patent issuing from this application because they are not true publications.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite because of the recitation, "..wherein the second cell or tissue is of one cell type or of different cell types..". The instant claim depends from claim 1, which is drawn to 2 cells types wherein the 1st cell type is different from the 2nd

cell type. It is unclear if claim 12 is now drawn to 2 cell types ***OR*** 3 (or more) cell types. Clarification is requested.

Claim 31 recites the limitation "..the process according to claim 21, wherein in step (b)..". There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

Claims 8 and 11 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 3 and 1, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). If the claims are not of similar scope, Applicant is asked to specifically point in the specification, the patentable distinction between the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6, 9-34, 36, 37, 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Maxwell et al., (reference submitted by Applicant; PNAS, Vol. 90, pages 2423-2427, March 1993).

The Examiner notes that claim 1 does not require that the at least one first cell/tissue type and the at least second cell/tissue type, wherein the first cell/tissue type is different from the second cell/tissue type be in the same petri dish or flask. Claim 1 encompasses first and second different cell/tissue types producing EPO in the culture medium independently of each other (i.e. the different cell/types can be in separate cultures/flasks). The instant claim also encompasses the first and second different cell/tissue types producing EPO in the culture medium, wherein first cell/tissue type is stimulated to induce the production of the second cell/tissue type. (i.e. co-cultured or mixed together).

Maxwell et al. teach that EPO synthesis is induced by reduction of blood oxygen availability and that the EPO gene is expressed in subsets of cells in kidney and liver. Maxwell et al. state that Hep3B and HepG2 cell lines demonstrated that both oxygen sensing and EPO production could occur in the same cell (page 2423, 1st-2nd paragraph). Maxwell et al. teach that to examine other cells for oxygen-sensing properties, the EPO 3' enhancer was coupled to alpha1-globulin promoter (Figure 1). Maxwell et al. teach the transfection of human hepatoma, human fetal lung fibroblast, human skin fibroblast, human monocyte/macrophage, monkey renal fibroblast, pig renal epithelium, rat aortic endothelium, Chinese hamster fibroblast, Chinese hamster ovary and mouse renal adenocarcinoma with the instant plasmid **(applies to claims 9-14 and 37)**. Maxwell et al. teach that the physiological characterization of the hypoxic response observed shows features strikingly similar to those previous established for the native EPO gene. Maxwell teach that hypoxic induction via the EPO 3' enhancer was

demonstrated in 11 of the 12 cells lines (page 2423, 3rd-4th paragraph and page 2424, 1st full paragraph and Table 1)**(applies to claim 6)**. Maxwell et al. teach that cells transfected with the plasmids were incubated in parallel in normoxia and hypoxia conditions (Table 1)**(applies to claim 34)**. Transfected cells were incubated in 100-mm petri dishes covered with 8 mls of culture medium. The hypoxic incubation was 1% O_2 with 5% CO_2, 94% N_2 in a Napco 7100 incubator (experimental incubation conditions; page 2423). Thus the transfected cells are cultured in petri dishes in an incubator. Identical cells are in a shared petri dish. The 12 cell lines are in a shared incubator. The Napco 7100 incubator allows the diffusion of gas molecules **(applies to claims 19-28, 30-32, 36, 39 and 40)**. Maxwell et al. teach that in two experiments at 0.1% O2, inducibility was greater than that seen at 1% O2 (page 2424, last paragraph-page 2425)**(applies to claim 29)**. Maxwell et al. teach the transfection of the different cells types with the mouse EPO gene and the EPO 3' enhancer. The RNase protection assay demonstrates the expression of transfected mouse EPO genes in Hep3B and CHO cells lines (page 2425, 2nd full paragraph) **(applies to claims 15-18)**. Maxwell et al. teach endogenous EPO gene expression from hypoxically stimulated hepatoma cells (page 2425, 2nd column, 1st paragraph)**(applies to claims 1, 2, 9 and 33)**. Maxwell et al. teach that cobalt induces native EPO gene expression in hepatoma cells. Maxwell et al. teach that in Chinese hamster lung fibroblastoid, the transfected EPO enhancer was activated by cobaltous ions **(applies to claim 5)**.

Claims 1, 3, 4, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ascensao et al. (Blood, Vol. No. 5, pages 1132-1134; November 1983).

Ascensao et al. teach a human testis germ cell line (1411-H cells) that produces EPO. Ascensao et al. teach 1411-H cells as a mixed testicular germ cell tumor derived from a metastatic human tumor (page 1133, 2nd column, 1st full paragraph). Ascensao et al. teach that the supernatant from the testis germ cell line stimulated and sustained the formation of erythroid colonies by sheep marrow erythroid progenitors (CFU-E) *in vitro*. The 1411-H cells grew in an adherent layer supplemented with serum (page 1132, 3rd full paragraph). The cell supernatant was added to the CFU-E, which resulted in an increased number and size of CFU-E (page 1133, 1st full paragraph). Ascensao et al. teach that the *in vitro* erythroid-stimulating activities were neutralized by anti-EPO, further identifying it as EPO. Ascensao et al. teach that the availability of continuous cell lines that produces significant quantities of EPO would be of major value.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 35 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maxwell et al. as applied to claims 1 and 21 above, and further in view of Klaus et al., United States Patent Application Publication, US 2003/0153503 A1.

The teachings of Maxwell et al. are described above. Maxwell et al. do not teach factors in the culture medium or matrix/scaffolds.

Klaus et al. et al. teach methods of increasing endogenous EPO *in vitro* by incubating the cells in culture with compounds (abstract; para 0022 and 0025). Klaus et al. teach that the compounds of the invention can be administered in combination with factors such as exogenous EPO and/or G-CSF (para 0064). Klaus et al. teach cell culture techniques are generally available in the art. Cells may be in suspension, attached to substrate, etc. EPO produced by the cells is secreted into the culture medium, collected and purified.

It would have been obvious to one of skill in the art at the time the invention was made to modify the method of preparing/isolating EPO as taught by Maxwell et al. by including various cell culture substrates as taught by Klaus et al. with a reasonable expectation of success. The motivation and expected success is provided by Maxwell and Klaus. Maxwell et al. teach methods of producing EPO *in vitro*. Klaus et al. teach

other ways of cell culture techniques to produce EPO, which is routine optimization and well within the purview of the skilled artisan.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/

Primary Examiner, Art Unit 1647

/R. M. D./
Examiner, Art Unit 1647
2/26/10